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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,435	11/26/2003	Weihong Xiong	01121-17272	6215

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,435	XIONG ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-97* is/are pending in the application.

4a) Of the above claim(s) *53-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *81-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *08/30/04* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The receipt is acknowledged of applicants' election filed 06/29/2006.

Election/Restrictions

1. Applicant's election without traverse of Group III claims 81-97 in the reply filed on 06/29/2006 is acknowledged.

2. Claims 53-80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups I, and II, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/29/2006.

Claims 81-97 are included in the prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 82, 87-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 82, the expressions "salts, analogs, derivatives and prodrugs" do not set forth the metes and bounds of the claim. Recourse to the specification does not define the expressions.

Claim 87 recites "the method further comprising a hormone", and this is confusing because how the method will comprise a hormone? And where the hormone is present, is it in the transdermal device or is administered separately by any other means?

With regard to claim 90, the claim recites "the method further comprising a treatment agent", and this is confusing because how the method will comprise a treatment agent? And where the treatment agent is present, is it in the transdermal device or is administered separately by any other means?

Regarding claim 94, the claim recites "the method further comprising co-administering a positive health benefit imparting substance", and this is confusing because how this co-administrating step is performed? is it by the same transdermal device or is administered separately by any other means?

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 81-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US 6,352,715 ('715) with the effective filing date February 19, 1998.

US '715 teaches a transdermal drug delivery system to administer huperzine A in a controlled release skin patch designed for once-a-week application to treat Alzheimer disease (AD) (abstract; col.3, lines 55-65; col.4, lines 7-15; col.9, lines 1-7, 31).

However, US '715 does not teach the blood plasma levels of huperzine provided by the transdermal system as instantly claimed.

The blood plasma levels are controlled by the amount of the drug included in the system as well as by the ingredients of the transdermal formulation used to deliver the huperzine such as the type of the adhesive, the permeation enhancers and other additives in the formulation.

Therefore, the claimed blood plasma levels of huperzine can be determined by one having ordinary skill in the art by manipulating the transdermal formulation

containing the huperzine and the structure of the transdermal device delivering it. Additionally, individual patient need is also a controlling factor in determination of the dose of huperzine.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD as disclosed by US '715, and manipulate the amount of huperzine and the formulation containing it, as well as the structure of the transdermal delivery system motivated by the specific individual patient need to achieve the desired results, with reasonable expectation of having transdermal delivery system that provides the desired blood plasma levels of huperzine to treat the AD patients with great success. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 105 USPQ 233.

8. Claims 81-86, 90, 93-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,159,986 ('986).

US '986 teaches a therapies and compounds for the inhibition of memory loss and treatment for AD, i.e. cognitive impairment, comprising transdermal administration of huperzine A in combination with hypericin, which is an antidepressant (abstract; col.2, lines 6-20, 62). Other ingredients may be added to huperzine to tune performance of the therapy including antioxidants, amino acids, and vitamins (col.3, lines 8-18). US '986 further teaches that hypericin is commercially available over the counter supplement

making the treatment of memory impairment an attractive low cost approach to treatment of the deleterious effects of memory loss (col.1, lines 7-10, 42-50).

However, US '986 does not teach the blood plasma levels of huperzine provided by the transdermal system as instantly claimed.

The blood plasma levels are controlled by the amount of the drug included in the system as well as by the ingredients of the transdermal formulation used to deliver the huperzine such as the type of the adhesive, the permeation enhancers and other additives in the formulation.

Therefore, the claimed blood plasma levels of huperzine can be determined by one having ordinary skill in the art by manipulating the transdermal formulation containing the huperzine and the structure of the transdermal device delivering it. Additionally, individual patient need is also a controlling factor in determination of the dose of huperzine.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver huperzine transdermally to patients suffering from memory loss along with hypericin, amino acid and vitamins as disclosed by US '986, and manipulate the amount of huperzine and the formulation containing it, as well as the structure of the transdermal delivery system motivated by the specific individual patient need to achieve the desired results, with reasonable expectation of having transdermal delivery system that provides the desired blood plasma levels of huperzine to treat the AD patients with great success. It has been held that where the general conditions of a

claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 105 USPQ 233.

9. Claims 81, 83-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over CN 1111987 ('987).

CN '987 teaches a plaster for treating senile dementia with long activity life of 3-4 days comprising huperzine (abstract). CN '987 teaches the plaster containing adhesive layer containing 0.1 to 8% w/w of huperzine, and applicants used in all their examples 0.01 to 20% w/w of huperzine. Therefore, it is expected that the same amount of huperzine disclosed by the prior art to provide the same blood plasma level of huperzine if it is present in the same formulation.

CN '987 does not teach explicitly teach the blood plasma levels of huperzine provided by the transdermal system as instantly claimed, however, it is expected that the plaster disclosed by CN '987 to provide the same blood plasma level of huperzine because it contains the same amount of the huperzine.

The plasma levels are controlled by the amount of huperzine included in the system as well as by the ingredients of the transdermal formulation used to deliver the huperzine such as the type of the adhesive, the permeation enhancers and other additives in the formulation.

Therefore, the claimed blood plasma levels of huperzine can be determined by one having ordinary skill in the art by manipulating the transdermal formulation containing the huperzine and the structure of the transdermal device delivering it.

Additionally, individual patient need is also a controlling factor in determination of the dose of huperzine.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver huperzine transdermally to treat senile dementia as disclosed by CN '987, and manipulate the amount of huperzine and the formulation containing it, as well as the structure of the transdermal delivery system motivated by the specific individual patient need to achieve the desired results, with reasonable expectation of having transdermal delivery system that provides the desired blood plasma levels of huperzine to treat the AD patients with great success. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 105 USPQ 233.

10. Claim 82 is rejected under 35 U.S.C. 103(a) as being unpatentable over CN '987 in view of US '715.

The teachings of the references are discussed above.

However, CN '987 does not teach huperzine A as claimed in claim 82, which is taught by US '715.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat senile dementia with plaster comprising huperzine as disclosed by CN '987, and use huperzine A as taught by US '715, motivated by the teaching of US '715 that huperzine A is naturally occurring acetylcholine esterase

inhibitor that traditionally used to alleviate memory problem, with reasonable expectation of having plaster comprising huperzine A that effectively alleviate memory problems in patients in need of such treatment.

11. Claims 90, and 93-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '715 or CN '987 in view of US '986.

The teachings of the references are discussed previously.

US '715 and CN '987 both teach treating cognitive dysfunction using huperzine administered transdermally.

However, US '715 and CN '987 do not teach administering treatment agent such as antidepressant as claimed in claims 90 and 93, or the co-administration of positive health benefit imparting substance as claimed in claims 94-97, which are all taught by US '986.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver huperzine transdermally to treat cognitive dysfunction as disclosed by any of US '715 or CN '987, and further add hypericin as disclosed by US '986, motivated by the teaching of US '986 that hypericin is commercially available over the counter and it makes the treatment of memory impairment an attractive low cost approach for treatment of the deleterious effects of memory loss, and additionally, one having ordinary skill in the art would have been motivated to administer antioxidants, amino acids, and vitamins to patient with cognitive dysfunction motivated by the teaching of US '986 that antioxidants, amino acids and vitamins tune the performance of

the huperzine therapy, with reasonable expectation of treating cognitive dysfunction using transdermal huperzine associated with available low cost hypericin, antioxidant, amino acids, and vitamins so that the deleterious effects of memory loss is treated and the performance of the AD therapy is tuned.

12. Claims 87-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '715, US '986 or CN '987 each in view of US 6,524,616 ('616).

The teachings of US '715, US '986 and CN '987 are discussed above.

However, the references do not teach administration of hormones with huperzine to treat cognitive dysfunction as claimed in claims 87-89.

US '616 teaches composition for improving cognitive function and memory in mammals with disorders associated with memory impairment. The composition comprises huperzine A and estrogen in combination to reduce loss of cholinergic neurons and to improve cognitive function and memory (abstract; col.9, lines 52-60; col.13, lines 17-25, 54-60). The composition is suitable for treating individuals with the risk of developing AD, aging associated cognitive disorders, and dementia (col.9, lines 60-65). The composition can be administered by transdermal routes (col.11, line 29; col.13, line 36).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by any of US '715, US '986 and CN '987, and further add estrogen to the transdermal formulation or co-administer estrogen to the patient as

disclosed by US '616, motivated by the teaching of US '616 that combination of huperzine and estrogen reduces loss of cholinergic neurons, improves cognitive function and memory and treats individuals with the risk of developing AD, aging associated cognitive disorders, and dementia, with reasonable expectation of treating cognitive dysfunction using transdermal delivery system comprising huperzine associated with estrogen administration to reduce loss of cholinergic neurons, improve cognitive function and memory and to treat individuals with the risk of developing AD, aging associated cognitive disorders, and dementia with great success.

13. Claims 87-90, 94, 95 and 97 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '715 or CN '987 each in view of the article "Drug Treatment for Alzheimer's Disease" by Tiffany et al.

The teachings of US '715, US '986 and CN '987 are discussed above.

However, the references do not teach administration of hormones with huperzine to treat cognitive dysfunction as claimed in claims 87-89, administration of treatment agent as claimed in claim 90, administration of vitamin or antioxidant as claimed in claims 94, 95 and 97.

Tiffany et al. teach the treatment of AD with cholinesterase inhibitor is associated with symptoms-appropriate psychotropic medication to slow the progression of the disease. Tiffany et al. teach administration of neuroprotective agents to prolong disability and caregiver burden instead of preserving function, such neuroprotective agents include antioxidants, such as vitamin E, to slow the decline of cognition and

functional ability and to prolong the time of death. Another neuroprotective agent is estrogen that is proven to be beneficial for depressed mood and memory impairment (see the provided article).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by any of US '715 and CN '987, and further add the appropriate psychotropic medication as disclosed by Tiffany et al. to provide appropriate symptomatic treatment, motivated by the teaching of Tiffany et al. that such psychotropic agents slow the progression of the disease, with reasonable expectation of treating AD using huperzine associated with psychotropic agent to slow the progression of the disease. Additionally, one having ordinary skill in the art at the time of the invention would have been motivated to co-administer neuroprotective agents with the huperzine such as antioxidant vitamins and estrogen as disclosed by Tiffany et al., motivated by the teaching of Tiffany et al. that neuroprotective antioxidant vitamins slow the decline of cognition and functional ability and prolong the time of death, and motivated by the teaching of Tiffany et al. that estrogen is proven to be beneficial for depressed mood and memory impairment, with reasonable expectation of treating AD using tansdermal huperzine, antioxidant vitamins, and estrogen with slowing of cognitive decline and memory impairment, as well as improvement of depressed mood associated with AD.

14. Claims 87-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '986 in view of Tiffany et al.

The teachings of the references are discussed above.

US '986 does not teach estrogen to treat AD, which is taught by Tiffany et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by US '986, and further co-administer estrogen with the huperzine as disclosed by Tiffany et al., motivated by the teaching of Tiffany et al. that estrogen is proven to be beneficial for depressed mood and memory impairment, with reasonable expectation of treating AD using huperzine and estrogen with improving of depressed mood and memory impairment associated with AD.

15. Claims 90 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '715 and CN '987 each in view of 5,104,880 ('880).

The teachings of US '715 and CN '987 are discussed above.

However, the references do not teach treatment agent selected from antipsychotic, anxiolytic or antidepressant as claimed in claims 90 and 93.

US '880 teaches huperzine to treat AD and memory disorders in combination with antidepressant drugs such as clonidine and desipramine, wherein the combination facilitates acetyl choline release and constitutes effective therapeutic strategy (col.3, lines 25-41). The reference teaches composition comprising the huperzine and antidepressant that can be administered topically (col.10, lines 1-2).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by any of US '715 and CN '987, and further add antidepressant as disclosed by US '880, motivated by the teaching of US '880 that the combination of huperzine and antidepressant facilitates acetyl choline release and constitutes effective therapeutic strategy for treating AD and memory disorders, with reasonable expectation of treating cognitive dysfunction using effective therapeutic strategy comprising administering huperzine and antidepressant for treating AD and memory disorders with great success.

16. Claims 90 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '715 and CN '987 each in view of US 5,877,173 ('173).

The teachings of US '715 and CN '987 are discussed above.

However, the references do not teach treatment agent selected from antipsychotic, anxiolytic or antidepressant as claimed in claims 90 and 91.

US '173 teaches method for reducing progressive neuronal degeneration due to AD using antipsychotic drugs (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by any of US '715 and CN '987, and further add antipsychotic drug as disclosed by US '173, motivated by the teaching of US '173 that antipsychotic reduces progressive neuronal degeneration due to AD, with reasonable

expectation of treating AD using huperzine associated with antipsychotic drug with reduction of progressive neuronal degeneration caused by AD.

17. Claim 91 is rejected under 35 U.S.C. 103(a) as being unpatentable over US '986 in view of US '173.

The teachings of the references are discussed above, US '986 teaches antidepressant associated with huperzine therapy to treat AD, but does not teach antipsychotic as claimed in claim 91, which is taught by US '173.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by US '986, and replace the antidepressant with an antipsychotic drug as disclosed by US '173, motivated by the teaching of US '173 that antipsychotic reduces progressive neuronal degeneration due to AD, with reasonable expectation of treating AD using huperzine associated with antipsychotic drug with reduction of progressive neuronal degeneration caused by AD.

18. Claims 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '715 or CN '987 each in view of US 5,668,117 ('117).

The teachings of US '715 and CN '987 are discussed above.

However, the references do not teach treatment agent selected from antipsychotic, anxiolytic or antidepressant as claimed in claims 90 and 92.

US '117 teaches the treatment of AD can be improved by administration of antipsychotic drugs and anxiolytic drugs along with huperzine (col.30, example 2, lines 28-30; col.32, lines 5-20, 46-47; col.33, lines 30-32).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by any of US '715 and CN '987, and further add antipsychotic and anxiolytic drug as disclosed by US '117, motivated by the teaching of US '117 that such drugs improve the treatment of AD, with reasonable expectation of treating AD using huperzine associated with antipsychotic and anxiolytic drugs to improve the treatment of AD.

19. Claims 91 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '986 in view of US '117.

The teachings of the references are discussed above, US '986 teaches antidepressant associated with huperzine therapy to treat AD, but does not teach antipsychotic and anxiolytic drugs as claimed in claims 91 and 92, which are taught by US '117.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat cognitive dysfunction using transdermal patch comprising huperzine as disclosed by US '986, and replace the antidepressant with an antipsychotic or anxiolytic drug as disclosed by US '117, motivated by the teaching of US '117 that such drugs improve the treatment of AD, with reasonable expectation of

treating AD using huperzine associated with antipsychotic and anxiolytic drugs to improve the treatment of AD.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Isis Ghali
Examiner
Art Unit 1615

IG

Isis Ghali